Assessing the Rationale and Effectiveness of Frozen Plasma Transfusions

An Evidence-based Review

Alan Tinmouth, MD, MSc, FRCPC[a,b,c,*]

KEYWORDS

• Frozen plasma • Hemostasis • Bleeding • Prophylaxis • Appropriateness

KEY POINTS

- The primary indications for frozen plasma transfusions are the treatment and prevention of bleeding in patients with prolonged coagulation tests, but there is a lack of well-conducted clinical studies to determine the appropriate indications.
- Most patients with mild coagulation test abnormalities do not have a significant hemostatic defect and do not benefit from frozen plasma transfusions.
- No clinical studies have shown a benefit from prophylactic frozen plasma transfusions to nonbleeding patients or before invasive procedures.
- Early transfusion of frozen plasma in massive transfusions is important but current evidence does not support the use of fixed frozen plasma to red transfusion ratios.
- Inappropriate transfusion of frozen plasma is common and may result in adverse events.

Frozen plasma (FP) is a commonly used blood product. The primary indications for FP transfusions are reversal of coagulopathy and replacement fluid in plasma exchange. In the United States, more than 4 million units of FP are transfused annually.[1] In general, the evidence to support the use of FP is limited,[2–4] which has resulted in significant overuse of the product. This overuse likely results in increased adverse

Disclosures: A. Tinmouth is supported by a research award from the Department of Medicine, The Ottawa Hospital and is a medical consultant to the Canadian Blood Services. The research for this article was partially supported by grants from the Canadian Institutes of Research and the Canadian Blood Services (86459 and 102538).

[a] Department of Medicine, Ottawa Hospital, University of Ottawa, 501 Smyth Road, Ottawa, Ontario K1H 8L6, Canada; [b] Department of Pathology and Laboratory Medicine, Ottawa Hospital, University of Ottawa, 501 Smyth Road, Ottawa, Ontario K1H 8L6, Canada; [c] Clinical Epidemiology Program, University of Ottawa Centre for Transfusion Research, Ottawa Health Research Institute, 501 Smyth Road, Ottawa, Ontario K1H 8L6, Canada
* 501 Smyth Road, Ottawa, Ontario K1H 8L6, Canada.
E-mail address: atinmouth@ohri.ca

Hematol Oncol Clin N Am 30 (2016) 561–572
http://dx.doi.org/10.1016/j.hoc.2016.01.003 **hemonc.theclinics.com**
0889-8588/16/$ – see front matter

complications of FP. This article reviews the rationale for the use of FP and the evidence supporting the use and effectiveness of FP transfusions.

FROZEN PLASMA PRODUCTS

Plasma is collected as part of whole blood collections with subsequent separation by centrifugation or by apheresis technology. Within 8 hours of collection, plasma is designated as fresh FP (FFP). Most apheresis plasma is still FFP, but, currently, plasma from whole blood collection is most commonly frozen within 24 hours and referred to as FP-24. In addition, the demand for rapidly available plasma for patients with trauma has resulted in thawed FP being stored for up to 5 days before use. The levels of factor V and VIII decline during longer prestorage holds and after thawing, but adequate levels of all factors are maintained.[5,6] As a result, FFP, FP-24, and thawed plasma are largely used interchangeably in clinical practice. This article uses the term FP generically to refer to all plasma products unless specifically indicated.

More recently, virally inactivated plasma, either individual plasma units (methylene blue, amotosalen–ultraviolet A (UVA), riboflavin-UVA), or pooled solvent-detergent–treated plasma have become available. Laboratory studies show small differences in coagulation or inhibitory proteins in the various pathogen inactivated plasma products,[7–11] but the clinical studies performed to date have not shown any differences in clinical efficacy.[12–15]

RATIONALE FOR FROZEN PLASMA USE

A simple paradigm for the use of FP to treat or prevent bleeding has been described[16,17]: (1) abnormal coagulation tests represent a decrease in levels of coagulation factors that could contribute to bleeding; (2) FP transfusions increase the levels of coagulation factors and correct the coagulation test abnormalities; (3) the correction of the coagulation test abnormality decreases bleeding (**Fig. 1**). However, there are important limitations to each of these 3 tenets.

A prolonged or abnormal coagulation test may not reflect a clinically significant reduction in the coagulation factor levels. Decreases in coagulation factor levels prolong either the activated partial thromboplastin time (aPTT) and/or the prothrombin time, commonly reported as the International Normalized Ratio (INR), but the risk of

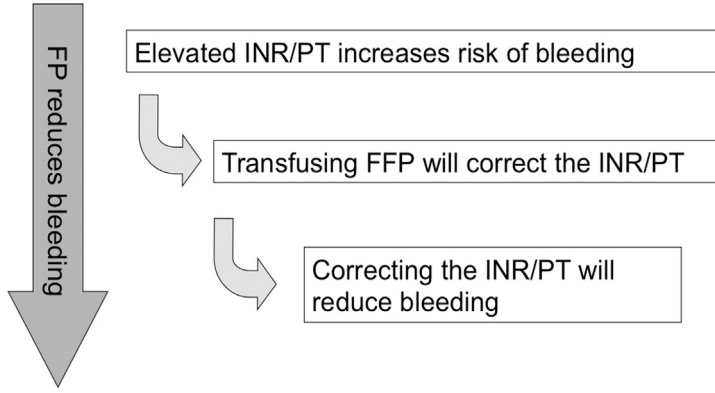

Fig. 1. Paradigm for the use of FP to treat or prevent bleeding. (*From* Tinmouth A. Evidence for a rationale use of frozen plasma for the treatment and prevention of bleeding. Transfus Apher Sci 2012;46(3):294; with permission.)